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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,303	05/11/2007	Eric Kandel	70442-PCT-US/JPW/CH	3996

23432 7590 09/18/2008

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EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
09/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,303	KANDEL ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-17,19,20 and 26-28* is/are pending in the application.

4a) Of the above claim(s) *19,20,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12-17 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/8/6; 7/20/7*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal matters

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Election/Restrictions

2. Applicant's election with traverse of Group I in the reply filed on June 09, 2008 is acknowledged. The traversal is on the ground(s) that, "the claims of Groups I-IV are not independent. Under M.P.E.P. §802.1, "independent" means "there is no disclosed relationship between the subjects disclosed, that is, they are unconnected in design, operation, and effect...". The claims of Groups I-IV are related in that the pending claims are all drawn to methods or compositions relating to gastrin releasing peptide" (p. 8 of the Response). This is not found persuasive for the following reasons.

Pursuant to 37 C.F.R. § 1.475 (a), Unity of invention before the International Searching Authority, an international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior

art. As such, pursuant to 37 C.F.R. § 1.475 (b), the ISA/US considers that when an international or a national stage application containing claims to different categories of invention unity of invention exists if the claims are drawn only to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

In the instant case, the first claimed invention belongs to the category (4) process - method for treating a subject by administration of a receptor agonist. Neither of the inventions of Groups II or IV encompass "an apparatus or means specifically designed for carrying out the said process". Groups II and IV, claims 19-20 and 26-27, are directed to nucleic acids and transgenic animals, which do not correspond to the technical feature of the instant elected invention of Group I, thus representing independent and distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 19, 20, 26 and 27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 09, 2008.

4. Claims 1-10, 12-17 and 28 are under examination in the instant office action.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-10, 12-17 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 1 and 8 are vague and indefinite in so far as they employ the term "fear-related disorder" as a limitation. This term relates to psychiatric/mental disorder and appears to be novel because DSM-IV (Diagnostic and statistical manual of mental disorders, American Psychiatric Association) does not recognize the term "fear-related disorder". Because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "fear-related disorder" (see p. 13 at paragraph 25, "a "fear-related disorder" shall mean any disorder induced by or resulting from an event that causes apprehension or alarm in the afflicted subject"), an artisan cannot determine if a pathological condition which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

8. Similarly, claims 3-5, 7, 10 and 28 are vague and ambiguous for recitation of different psychiatric pathologies ("phobia", "chronic anxiety"), which are not clearly defined by the instant specification or reference to the art-accepted terms. In case of claim 7, relationship of "autism" with "fear-related disorders" is not obvious. Clarification is required.

9. The term "inhibiting" in claim 8 is a relative term which renders the claim indefinite in view of the absence of point of reference to ascertain the recited inhibition. Further, the metes and bounds of "inhibiting [...] the onset of a fear-related disorder" cannot be determined from the claim or the instant specification as filed.

10. Claims 2, 6, 9, 12-17 are indefinite for being dependent from indefinite claims.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-10, 12-17 and 28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-7 are directed to methods for treating fear-related disorders by administration of a gastrin releasing peptide receptor agonist. Claims 8-10, 12-17 and 28 encompass preventive measures to delay (inhibit) the onset of fear related disorders by administration of a gastrin releasing peptide receptor agonist. However, the instant specification fails to provide enough guidance how to practice the claimed methods, thus requiring undue experimentation on part of the skilled practitioner to research and discover how to practice Applicant's invention as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enablement scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification (see MPEP 2111 [R-1], which states that claims must be given their broadest reasonable interpretation

"During patent examination, the pending claims must be "given *>their< broadest reasonable interpretation consistent with the specification." *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969)".

As such, the broadest reasonable interpretation of the claimed methods is that administration of a gastrin releasing peptide receptor (GRPR) agonist allows treatment and prevention of different pathological condition generally named by Applicant as "fear-related disorders". The specification defines these disorders as "any disorder induced by or resulting from an event that causes apprehension or alarm in the affected subject" (p. 13). Treatment of autism is included within the claimed subject matter, see claim 7. Thus, the claims encompass an

unreasonable number of clinical conditions, which the skilled artisan would not know how to first distinguish as a "fear-related disorder" and then treat. As opposed to the claims, what is disclosed about the claimed method is narrow: studies of *GRP* gene expression (pp. 26-28) and behavioral experiments using GRPR-knockout mice (pp. 32-45). The specification fails to provide any factual evidence or present sound scientific reasoning to support a conclusion that GRPR-knockout mice represent an art-recognized animal model for fear-related disorders or that the aberrant behavior recorded in GRPR-deficient mice can be treated by administration of the deficient peptide.

The art recognizes that stressful stimuli evoke abundance of physiological responses, which involve activation of the sympathetic nervous system and of the hypothalamic-pituitary adrenal (HPA) axis. Gastrin-releasing peptide (GRP), which belongs to bombesin family of peptides known to contribute to the integration and/or mediation of the stress response, has been shown to have effect on emotionally-motivated memory, anxiety-like behaviors, conditioned fear, and neuroendocrine responses to stressors (see Wada et al., 1997, IDS of 7/20/07; Merali et al., 2000, IDS of 7/20/07; Yamada et al., 2000, Brain Res. 870, pp. 20-26; Iton et al., 1994, Jap. J. Physiol., 22, pp. 271-281). Administration of agonists of GRP, bombesin-like peptides and GRP itself, to animals with normal (not altered) genotype has been reported to lead to behavioral changes, not necessarily limited to fear-related responses (Iton et al, 1994). Article of Wada et al. specifically teaches that activation of GRP receptor elicits a wide spectrum of biological effects on behavior, digestion, and metabolism (see abstract, for example). Also, mice lacking GRP receptor have been shown to display aberrant behavior not associated with reduced anxiety (Yamada et al., 2000).

While the skill level in the art is high, the level of predictability is low. There are many clinical conditions that can be characterized as comprising fear-related responses, and many physiological pathways, which regulate responses related to stressful conditions. The sole working examples in the specification, as originally filed, pertain to studies of GRPR deficient mice. While it is not necessary that Applicant understands or discloses the mechanism by which the invention functions, in this case, in the absence of such an understanding, no extrapolation can be made of the results of behavioral studies of transgenic animals lacking GRP receptor to predicting administration of GRPR agonists to treat pathological conditions related to fear.

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation of success. In the instant case, Applicant's invention is predicated on a working hypothesis, which associates GRPR activation and GABAergic inhibition (p. 20), and results of experiments on mice lacking GRP receptor. Applicant further extrapolates this hypothesis and experimental results into clinical methods of GRPR agonist administration. Thus, it appears that Applicant provides a correlated finding (the finding), and then presents an invitation to experiment and discover what effects would administration of GRP receptor agonists have on a subject afflicted with a fear-related disorder, and then research for suitable routes and regimes of administration.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed methods without first making a substantial inventive contribution.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

14. Claims 1-10, 12-17 and 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Shumyatsky et al., 2002 (reference 4 of IDS of 06/08/2006).

Claims 1-10, 12-17 and 28 lack novelty over the Shumyatsky et al. reference (published by "another") because a reference need not have described an actual reduction to practice of an

invention in order to serve as an anticipatory reference. See *In re Siveramakrishnan*, 673 F.2d 1383, 1384, 213 USPQ 441, 442 (CCPA 1982); *In re Donohue*, 766 F.2d 531, 533, 226 USPQ 619, 621 (Fed. Cir. 1985). Moreover, even if a reference does not explicitly set forth every element of the claim, the reference may still be an anticipatory reference if the element is inherent in the disclosure. See *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950 (Fed Cir 1999). In the instant case the Shumyatsky et al. reference explicitly teaches all that is disclosed in the instant specification. Because the instant specification is not enabling for the treatment of fear-related disorders by administration of GRPR agonists, disclosure of Shumyatsky et al. is anticipatory for disclosing the same amount of information, which is disclosed in the instant specification to support the claimed invention.

Conclusion

15. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Olga N. Chernyshev, Ph.D./
Primary Examiner, Art Unit 1649